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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,794	10/05/2001	Jennifer L. Hillman	PF-0565 USN	4717

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Incyte Genomics Inc
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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,794	HILLMAN ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,27-32 and 34-45* is/are pending in the application.

4a) Of the above claim(s) *21,31 and 34-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-30,32 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 21, 27-32, and 34-45 are pending in the application.

[2] Applicant's amendment to the claims filed February 11, 2004 is acknowledged. This listing of the claims replaces all prior versions and listings of the claims in the instant application.

[3] Applicants' amendment to the specification filed February 11, 2004 is acknowledged. Applicants' amendment replaces original Tables 1-4 of the specification and corrects the numbering of sequence identifiers such that a nucleic acid sequence identifier corresponds to the correct encoded polypeptide sequence identifier.

[4] Receipt of a computer readable form of a substitute sequence listing, a paper copy thereof, and a statement of their sameness, filed February 11, 2004, is acknowledged.

[5] Receipt of two (2) Declarations under 37 CFR 1.132, filed February 11, 2004 is acknowledged.

[6] Applicant's arguments filed February 11, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

[7] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Rejoinder

[8] Applicants' request for rejoinder of claims 34-36 and 43-44 as allegedly being drawn to methods of using the polynucleotide of elected Group XXXVIII is acknowledged. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. As the claims of Group XXXVIII are not yet allowable for the reasons of record and those reasons stated below, rejoinder is not yet required. If the polynucleotide of Group XXXVIII is found to be allowable, withdrawn claims will then be evaluated for rejoinder according to MPEP § 821.04.

Lack of Unity

[9] Applicants' request for withdrawal of the lack of unity requirement between claims drawn to polynucleotides and polypeptides is acknowledged. Applicants argue that the lack of unity of invention requirement should be withdrawn as unity of invention exists between the claims drawn to polynucleotides and polypeptides encoded thereby. Applicants' argument is not found persuasive.

As stated in a previous Office action, according to PCT Rule 13.2, unity of invention exists only when there is a shared same or corresponding special technical feature among the claimed inventions. The polynucleotide of claim 32 part b), which is

drawn to an isolated polynucleotide comprising a polynucleotide sequence at least 90% identical to SEQ ID NO:37, encompasses polynucleotides that, when expressed, result in the production of proteins that do not correspond to the polypeptide of claim 21. Therefore, the polynucleotide of Group XXXVIII, particularly the polynucleotide of claim 32 part b), does not share a corresponding special technical feature with the polypeptide of claim 21, and thus the inventions share no corresponding special technical feature and consequently do not have unity of invention.

[10] Claims 21, 31, and 34-44 are withdrawn from further consideration pursuant to 37 CFR § 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

[11] Claims 27-30, 32, and 45 are being examined on the merits.

Sequence Compliance

[12] In order to correct the numbering of sequence identifiers in the "Sequence Listing" such that the nucleic acid sequence identifier corresponds to the correct encoded polypeptide sequence identifier (see item [3] of the Office action mailed October 09, 2003), applicants have submitted a substitute sequence listing. However, the amendment fails to comply with 37 CFR § 1.825(a), which requires a statement that the substitute sheets include no new matter. In order to comply with the sequence requirements, applicants are required to submit a statement that the substitute sheets include no new matter.

Oath/Declaration

[13] The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: the filing dates of the provisional applications stated in the declaration do not correspond to those stated in the first paragraph of the specification, which applicants assert to be correct (see item II at page 9 of the amendment filed February 11, 2004). The examiner objected to the specification in the Office action mailed October 09, 2003 as the filing dates of provisional applications to which applicants claim priority in the first paragraph of the specification are different from those filing dates of provisional applications to which applicants claim priority in the Declaration (see item [9] of the Office action mailed October 09, 2003). Applicants submit that the filing dates of the provisional applications are correct in the specification and state that a substitute Declaration can be obtained if necessary (see page 9, top of the response filed February 11, 2004). A substitute Declaration is required that correctly states the filing dates of the provisional applications to which applicants claim priority.

Specification/Informalities

[14] In view of applicants' explanation, asserting that the filing dates of the priority documents, as disclosed in the amendment to the specification, filed July 16, 2003, are correct, the objection to the specification as set forth in item [9] of the Office action mailed October 09, 2003 is withdrawn.

[15] The specification is objected to because SEQ ID NO:31 is referred to therein as a polypeptide sequence (see, *e.g.,* page 3, lines 23-24 of the specification), however the paper copy of the sequence listing indicates that SEQ ID NO:31 is a nucleic acid sequence. Also, the specification indicates that there are 62 sequence identifiers (see, *e.g.,* page 4, line 14 of the specification), however, the paper copy of the sequence listing has only 60 sequence identifiers. It is suggested that, for example, applicants replace "SEQ ID NO:1-31" with "SEQ ID NO:1-30" and replace "SEQ ID NO:32-62" with "SEQ ID NO:31-60" throughout the specification.

Claim Objections

[16] In view of applicants' amendment to the claims, the objection to claims 24-30, 32, 33, and 45 as set forth in item [10] of the Office action mailed October 09, 2003 is withdrawn.

Claim Rejections - 35 USC § 101

[17] The rejection of claims 27-30, 32, and 45 under 35 U.S.C. 101 is maintained for the reasons of record as set forth in item [11] of the Office action mailed October 09, 2003 and for the reasons stated below. The examiner maintains the position that the claimed invention is not supported by either a specific and substantial asserted utility or well-established utility.

Applicants assert the claimed polynucleotide corresponds to a phosphatidyl-inositol 3-kinase that is expressed in various human tissues. However, it should be

noted that the specification fails to expressly state that the polynucleotide of SEQ ID NO:37 encodes a polypeptide having phosphatidyl inositol-3 kinase activity. Instead, the specification merely indicates that the polypeptide encoded by SEQ ID NO:37 is "homologous" to a phosphatidyl-inositol 3-kinase without providing any evidence as to the level of amino acid sequence homology (see page 54 of the instant specification). As such, the examiner has not interpreted the specification's assertion that the polypeptide encoded by SEQ ID NO:37 is "homologous" to a phosphatidyl-inositol 3-kinase as meaning the encoded polypeptide exhibits phosphatidyl-inositol 3-kinase enzymatic activity.

Applicants argue the claimed invention has utility in toxicology testing, drug development, and disease diagnosis, which do not require knowledge of how the encoded polypeptide functions. In support of their argument, applicants submit two declarations under 37 CFR 1.132 (referred to by applicants as the "Rockett Declaration" and the "Iyer Declaration") and ten references. Applicants argue that these Declarations and references demonstrate that, at the time of filing the instant application, it was well-established that: 1) expressed polynucleotides can be used as hybridization probes to measure the presence, absence and amount of their cognate gene; 2) expressed polynucleotides produce a gene-specific expression signal under conditions that can be routinely established; 3) expression analysis is useful in drug discovery, toxicology, and phenotype characterization and categorization; 4) each additional gene-specific probe gives a more useful expression pattern; 5) biologists want each newly identified expressed gene to be included in such an analysis; 6) nucleic acid microarrays increase

parallelism of expression measurements with increased throughput; 7) each additional expressed gene in a microarray increases detection range and versatility; 8) biologists want a gene-specific probe to each expressed gene to be included in a microarray; 9) industrial suppliers of microarrays strive to improve microarray salability by adding an expressed gene to their microarrays; 10) biological function of a gene is not required to measure its expression; 11) failure of a probe to detect cognate gene expression changes does not diminish its usefulness; and 12) complete failure of a probe to detect its cognate transcript in an expression analysis experiment does not deprive the probe of utility to those who would use it as a research tool. Applicants' argument is not found persuasive.

Applicants' evidence allegedly demonstrating patentable utility has been fully considered. However, this evidence is found unconvincing. MPEP § 2107.01 states, "A 'specific utility' is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention" (italics in original). Expressed polynucleotides have a variety of general uses, *e.g.,* as a probe for hybridization or as a template for protein expression – these uses are applicable to *any* expressed polynucleotide and are not specific to the claimed polynucleotide. In this case, any expressed polynucleotide can be used as a hybridization probed in gene expression monitoring. Consequently, this asserted utility is not specific. MPEP § 2107.01 states, "Utilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities". Because the specification fails to provide guidance to allow a skilled artisan to use data

relating to the claimed polynucleotide derived from the results of gene expression analysis and what the results would mean, the results of gene expression monitoring assays would be meaningless without further research. In this case, the asserted use of the claimed polynucleotide for gene expression monitoring would be an assay to measure a polynucleotide that itself has no specific and substantial utility. Such a utility is not substantial as evidenced by MPEP § 2107.01, which provides the following example of a utility that is not substantial: "A method of assaying for or identifying a material that itself has no specific and/or substantial utility". Consequently, the claimed polynucleotide has no specific and substantial utility.

Applicants argue the examiner does not dispute that the claimed polynucleotide can be used as a probe in cDNA microarrays and used in gene expression monitoring. Applicants argue the examiner contends that the claimed polynucleotide cannot be useful without knowledge of its biological function or the function of the polypeptide encoded thereby. Applicants argue the law has never required knowledge of biological function to prove utility as it is the invention's use not its function that is the subject of the utility requirement. Applicants argue that, as demonstrated by the Rockett Declaration and the Iyer Declaration, a skilled artisan can achieve beneficial results from the claimed polynucleotide in the absence of knowledge of its biological function as the asserted uses are independent of its biological function. Applicants' arguments are not found persuasive.

There is no dispute that the claimed polynucleotide can be used as a probe as any expressed polynucleotide can be used as a probe, i.e., this use applies to the

general class of expressed polynucleotides and is not specific to the claimed polynucleotide. Contrary to applicants' assertion, the examiner acknowledges that the utility requirement does not require knowledge of a polynucleotide's biological function or the biological function of the corresponding encoded polypeptide. A claimed polynucleotide can meet the requirements of utility as long as the specification discloses a credible, specific and substantial asserted utility or a well-established utility for the claimed polynucleotide, even though the function of the polynucleotide or encoded polypeptide is not disclosed in the specification. For example, Shattuck-Eidens et al. (US Patent 5,693,473) teach mutant alleles of the *BRCA1* gene that predispose a patient to developing breast and ovarian cancers (abstract). While there is no disclosure of the function of the mutant *BRCA1* genes or their gene products, the invention nonetheless has utility as being an indicator for susceptibility to developing breast and ovarian cancers. Furthermore, and in contrast to the example of Shattuck-Eidens et al., further research is clearly required to allow a skilled artisan to use data relating to the claimed polynucleotide derived from the results of gene expression analysis and therefore, the asserted utility is not substantial.

Claim Rejections - 35 USC § 112, Second Paragraph

[18] In view of applicants' amendment to the claims, the rejection of claims 24, 28-30, and 32-33 under 35 U.S.C. 112, second paragraph, as set forth in item [12] of the Office action mailed October 09, 2003 is withdrawn.

[19] Claims 27-30 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

Claims 27, 28 (claim 29 dependent therefrom), 30, and 45 are confusing in that they are dependent upon claims that have been cancelled by amendment. Claims 27-30 are dependent upon cancelled claim 24 and claim 45 is dependent upon canceled claim 33. In the interest of advancing prosecution, claim 27 has been interpreted as an isolated polynucleotide comprising SEQ ID NO:37; claim 28 has been interpreted as being dependent upon claim 27; claim 30 has been interpreted as being dependent upon claim 27; and claim 45 has been interpreted as being dependent upon claim 32. It suggested that applicants clarify the meaning of the claims.

Claim Rejections - 35 USC § 112, First Paragraph

[20] The written description rejection of claims 32 and 45 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [13] of the Office action mailed October 09, 2003 and for the reasons stated below. The examiner maintains the position that the genus of claimed polynucleotides of claim 32 is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue the rejection is overcome by amendment to claim 21 to delete the "variant" and "fragment" language. Applicants' argument is not found persuasive.

Claim 32 (claim 45 dependent therefrom) is drawn to (in relevant part) a genus of polynucleotides comprising a naturally occurring sequence at least 90% identical to the polynucleotide of SEQ ID NO:37, a full complement thereof, and RNA equivalents thereof. The claimed genus encompasses species that are WIDELY variant in both structure and function, including (but not limited to) genomic sequences, allelic variants, and nucleic acid variants encoding polypeptides having function other than the activity of SEQ ID NO:7, e.g., non-functional polypeptides and polypeptides having activity other than the asserted kinase effector activity. MPEP § 2163 states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". As such, the disclosure of the single representative species of SEQ ID NO:37 is insufficient to be representative of the attributes and features of all species encompassed by the claimed genus of polynucleotides. Given the lack of description of a representative number of polynucleotides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention. Also, it is noted that the genus is limited to those variants that are "naturally occurring". MPEP § 2163 states (citing *Amgen*, 927 F.2d at 1206, 18 USPQ2d at 1021), "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials". In this case, the specification fails to provide those characteristics that distinguish a "naturally occurring" polynucleotide having at least 90%

identity to SEQ ID NO:37 from those polynucleotides that meet the sequence identity limitation, but are not "naturally occurring". For the reasons stated above, the specification fails to provide adequate written description for the claimed genus of polynucleotides.

[21] The enablement rejection of claims 27-30, 32, and 45 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [14] of the Office action mailed October 09, 2003 and for the reasons stated below. The examiner maintains the position that, since the claimed invention is not supported by either a substantial or specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants argue that, to the extent the instant rejection is based on the allegedly improper allegation of lack of patentable utility under 35 USC 101, the rejection fails for the same reasons. Applicants' argument is not found persuasive.

Applicants' arguments traversing the utility rejection under 35 USC 101 have been fully addressed above. To the extent those arguments apply to the instant rejection, the examiner maintains the instant rejection for those reasons stated in item [17] above.

[22] Even if applicants demonstrate the polynucleotide of SEQ ID NO:37 has a specific and substantial or well-established utility, the scope of enablement rejection of claims 32 and 45 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [15] of the Office action mailed October 09, 2003 and for the reasons stated below. The examiner maintains the position that the specification, while

being enabling for the polynucleotide of SEQ ID NO:37, does not reasonably enable all polynucleotides comprising a naturally occurring polynucleotide sequence at least 90% identical to SEQ ID NO:37.

Applicants argue the rejection is overcome by amendment to claim 21 to delete the "variant" and "fragment" language. Applicants' argument is not found persuasive.

Applicants' amendment fails to remove the "variant" and "fragment" language from claim 32 (claim 45 dependent therefrom), which recites a broad scope of polynucleotides "comprising a naturally occurring polynucleotide sequence at least 90% identical" to SEQ ID NO:37. The Factors of *In re Wands* that are most relevant to the instant rejection have been addressed in a prior Office action (see item [15] of the Office action mailed October 09, 2003). Applicants do not dispute the examiner's assertions that the claims are overly broad, the specification fails to provide the necessary guidance for making and using the broad scope of claimed polynucleotides, there is a high level of unpredictability in the art, and that an undue amount of experimentation is required to make and use the full scope of claimed polynucleotides. As such, undue experimentation is required for a skilled artisan to make and use the full scope of the invention.

Claim Rejections - 35 USC §§ 102 and 103

[23] In view of applicants' amendment to the claims, the rejection of claims 24 and 33 under 35 U.S.C. 102(a), the rejections of claims 24, 26, and 33 under 35 U.S.C. 102(b),

and the rejections of claims 28-30 under 35 U.S.C. 103(a), as set forth in items [16]-[21] of the Office action mailed October 09, 2003 are withdrawn.

Conclusion

[24] Status of the claims:

- Claims 21, 27-32, and 34-45 are pending.
- Claims 21, 31, and 34-44 are withdrawn from consideration.
- Claims 27-30, 32, and 45 are rejected.
- No claim is in condition for allowance.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman
Patent Examiner
Art Unit 1652
03-18-04